Disease free survival (DFS) in patients with resectable soft tissue sarcoma (STS) from EFTISARC-NEO phase II trial of neoadjuvant eftilagimod alfa (efti), pembrolizumab and radiotherapy (rth)

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BACKGROUND

- Eftilagimod alfa (efti) is a dimeric, soluble recombinant LAG-3 protein and MHC Class II agonist that stimulates antigen-presenting cells (APCs). The LAG-3 - MHC II interaction controls the signaling between T cells and APCs, which are responsible for the adaptive immune response.
- EFTISARC-NEO (NCT06128863) is a single-arm single-center phase II study evaluating neoadjuvant eftilagimod alfa combined with pembrolizumab and radiotherapy in patients with resectable STS.
- As presented at ESMO 2025 and CTOS 2025, **the study has met its primary endpoint, showing a median 51.5% of tumor hyalinization and fibrosis at the time of surgical resection**. Therapy was feasible, with all patients undergoing surgery without delays, and well tolerated. Grade3+ adverse events occurred in 20% of patients – 75% of which were related to postsurgical wound complications.

MATERIALS AND METHODS

Key Inclusion Criteria
- ≥ 18 years of age
- ECOG 0 or 1
- Primary or locally recurrent deep-seated extremities, girdles and/or superficial trunk (thoracic or abdominal wall) tumor
- Histologic diagnosis of STS except for Ewing Sarcoma, alveolar and embryonal rhabdomyosarcoma
- Grade 2 or 3 tumors according to FNCLCC
- Size of the primary tumor >5 cm or locally recurrent of any size;
- No distant metastases

Fig. 1. Scheme of treatment and diagnostic procedures in EFTISARC-NEO trial



Primary Endpoint :
- Percent tumor hyalinization and fibrosis as a marker of response to treatment assessed at the time of surgical resection – reported at ESMO 2025 and CTOS 2025

Key Secondary Endpoints:
- Disease-free survival (DFS),
- Locoregional disease-free survival (LRFS), Distant metastasis-free survival (DMFS),
- Overall survival (OS)

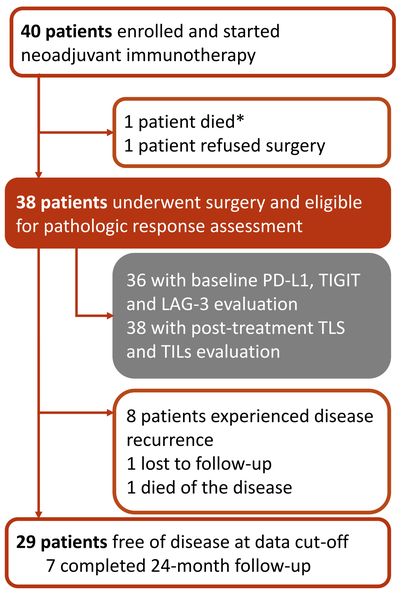
Exploratory Endpoints:
- Presence of tertiary lymphoid structures (TLS) assessed by expression of CD21 and CD23 by IHC in surgical specimen after treatment
- Presence of tumor infiltrating lymphocytes (TILs) measured by presence of CD3+ cells in surgical specimen after treatment
- Baseline expression of PD-L1, LAG-3 and TIGIT

Data cut-off : April 30, 2026

RESULTS

Patients' characteristics

Fig. 2. Patients' disposition



*due to SAE not related to therapy

Tab. 1. Patients' characteristics

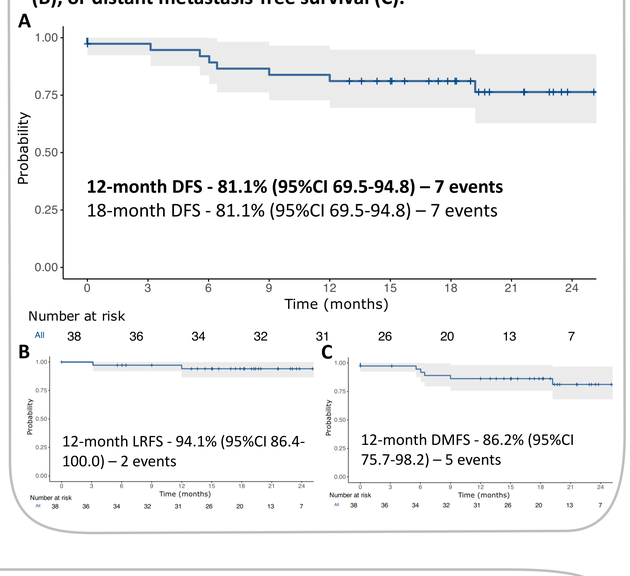
Characteristics		Patients, n=38
Female, % (n)		42.1% (16)
Median age, years (range)		54.5 (34-77)
Median tumor size, cm (IQR)		8.8 (6.7-10.9)
Recurrent tumor, % (n)		26.3% (10)
Tumor location, % (n)	Lower extremity	71.1% (27)
	Upper extremity	23.7% (9)
	Trunk	5.3% (2)
Subtype, % (n)	Myxofibrosarcoma	39.5% (15)
	Undifferentiated pleomorphic sarcoma	26.3% (10)
	Myxoid liposarcoma	13.2% (5)
	Dedifferentiated liposarcoma	5.3% (2)
	Malignant peripheral nerve sheath tumor	5.3% (2)
	Other*	10.5% (4)

* 1 each: synovial sarcoma, myxoid leiomyosarcoma, epithelioid sarcoma with TMEM123::YAP1 fusion, myxoinflammatory fibroblastic sarcoma

Survival outcomes

- Median follow-up: 19.1 months from surgery
- 8 patients experienced disease recurrence (2 local and 6 distant, with lung metastases in 4, bone metastases in 2, liver in 1)
- One patient died due to disease

Fig. 3. Disease-free survival (A), local recurrence-free survival (B), or distant metastasis-free survival (C).



Translational correlatives

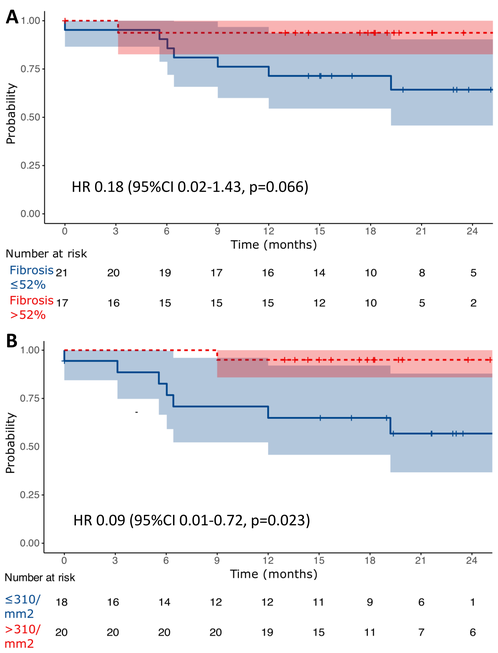
Tab. 2. Expression-of immune checkpoints at baseline, and presence of TILs after therapy

Characteristics		
PD-L1	*TPS , median (IQR)*	0 (0-1.5)
	Positive, % (n)	30.6% (11)
LAG-3	*Positive cells/mm², median (IQR)*	18 (2-51.5)
TIGIT	*high*	30.6% (11)
TILs	*CD3+ cells/mm², median (IQR)*	355 (178-618)

Tab. 3. Correlation of clinical and pathological factors with DFS

Characteristics		Events/total	1-year DFS	p
Grade	G2	5/23	78.3%	0.96
	G3	3/15	86.2%	
Subtype	Myxofibrosarcoma	3/15	86.2%	0.70
	Undifferentiated pleomorphic sarcoma	2/10	80.0%	
	Myxoid liposarcoma	1/5	80.0%	
	Other	2/8	75.0%	
Response (EORTC STBSG)	A	0/2	100%	0.56
	B	1/3	66.7%	
	C	4/13	75.0%	
	D	1/13	92.3%	
	E	2/7	71.4%	
TLS	absent	5/22	81.0%	0.77
	present	3/16	81.3%	

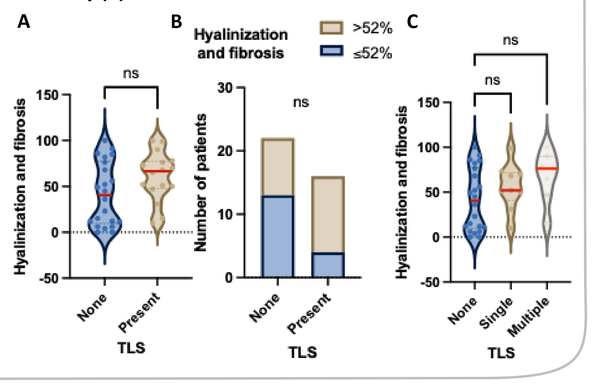
Fig. 3. DFS stratified by hyalinization/fibrosis at surgical specimen (A) and number of TILs after treatment (B).



Tab.4. Multivariate analysis of factors associated with DFS

Characteristics		Events/total	1-year DFS	HR (95%CI)	p
Hyalinization and fibrosis	≤52%	7/21	71.4%	1 (Ref)	0.139
	>52%	1/17	93.8%	0.21 (0.03-1.67)	
CD3+ TILs	≤310/mm²	7/18	64.9%	1 (Ref)	0.044
	>310/mm²	1/20	95.0%	0.12 (0.01-0.94)	

Fig. 4. Presence of TLS after treatment and correlations with hyalinization and fibrosis based on the presence (A, B) or maturity (C) of TLS.



CONCLUSIONS

- **EFTISARC-NEO trial shows promising long-term outcomes warranting further testing in late-stage neoadjuvant trials in patients with STS.**
- **12-month DFS was 81.1%, while 12-months LRFS and DMFS were 94.1% and 86.2%, respectively. Overall survival data are immature.**
- **High TIL infiltration after surgery and high levels of hyalinization and fibrosis after therapy emerge as potential prognostic factors, but longer follow-up is necessary.**
- **Baseline expression of PD-L1, LAG-3, TIGIT or presence of TLS do not correlate with preliminary survival outcomes.**
- **Translational studies revealed high frequency of TLS after therapy, suggesting potential induction of TLS formation by neoadjuvant therapy.**

FUNDING

Study is funded by grant from Medical Research Agency – agreement number 2022/ABM/01/00013-00. Immutep has provided eftilagimod alfa.

DISCLOSURES

Pawel Sobczuk: speaker honoraria – BMS, Swixx Biopharma, Gilead; travel grants – BMS, MSD, Novartis, Pierre Fabre; advisory board – Sandoz; Stocks owner – Celon Pharma; Board member - Polish Society of Clinical Oncology; **Tomasz Świtaj**: Speaker honoraria – BMS, MSD, Novartis, Pierre Fabre, Sanofi; travel grants – BMS, MSD, Novartis, Pierre Fabre; **Paweł Teterycz:** Speaker honoraria – BMS, MSD, Novartis, Pierre Fabre; travel grants – BMS, MSD, Novartis, Pierre Fabre; **Aneta Borkowska and Aleksandra Wiśniewska** declare no conflicts of interests; **Piotr Rutkowski:** Speaker honoraria – BMS, Merck, MSD, Novartis, Pierre Fabre, Sanofi; advisory board - Blueprint Medicines, BMS, Merck, MSD, Philogen, Pierre Fabre, Sanofi; research funding – BMS, Pfizer. **Katarzyna Kozak:** Speaker honoraria – BMS, MSD, Novartis, Pierre Fabre, Sanofi; advisory board - BMS, MSD;

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